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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,876	12/12/2001	Eileen White	RUT 98-0058	5628

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/25/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,876	WHITE ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph. D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *4-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group 1 (claims 1-3) in Paper No. 12 is acknowledged. The traversal is on the ground(s) that no lack of unity was identified in either Chapter 1 or Chapter II of the PCT. This is not found persuasive because of reasons set forth in the Restriction Requirement in Paper No. 11 and of the following reasons: A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to different categories (i.e., assessing promtor activity, binding between two different proteins, detecting a nucleic acid, a protein, or making protein in the instant application) are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said product; or (2) A product and a process of use of said product; or (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or (4) A process and an apparatus or means specifically designed for carrying out the said process; or (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group I will be the main invention. After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).) Groups II-V do not fall into any of (1)-(5) above.

The requirement is still deemed proper and is therefore made FINAL.

Claims 4-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claims 1-8 are pending and claims 1-3 are examined on merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

This rejection has many different aspects.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 recites "recombinant cell" but it is not clear what the metes and bounds are for the phrase.

Since the cell comprises the third plasmid expressing a selective marker gene and the specification at pages 22 and 23 indicates the purpose of the selective marker is to isolate a stably transfected cell line, this examiner will assume "a recombinant cell" means a stably transfected cell line. However, this treatment does not relieve applicant the burden of responding this rejection.

Claims 1-3 recite "p300" but it is not clear what the metes and bounds are for the term. Is a p300 a specific protein or a group of proteins as indicated from page 15 line 27 to page 16 line 20 of the specification? Since the specification says that mdm2 promoter is an example of p300-regulated promoter at page 22 lines 24 and 25 and Gu et al (June 19, 1997, Nature Vol. 387, pages 819-823) indicate mdm2 promoter is regulated by CBP, this examiner will assume the term "p300" is a group of protein the art recognize as p300/CBP transcriptional co-activators. Note page 15 line 27 to page 16 line 20 of the specification and Lill et al (June 19, 1997, Nature Vol. 387, pages 823-27). However, this treatment does not relieve applicant the burden of responding to this rejection.

Claims 1-3 recite "a p300 responsive promoter" but it is not clear what the metes and bounds are for the phrase. The specification from page 19-21 defines several

terms and phrases but does not define what is being claimed for patent protection by the phrase "a p300 responsive promoter". Is ***"the mdm2 promoter"*** at Figure 3 and page 820 left column line 11 from bottom of Gu et al (June 19, 1997, Nature Vol. 387, pages 819-823) within metes and bounds of "a p300 responsive promoter"?

Claims 1-3 recite "a non-p300 responsive promoter" but it is not clear what the metes and bounds are for the phrase. Is MG_{15}-CAT at page 823 right column line 23 and Figure 2 of Lill et al (June 19, 1997, Nature Vol. 387, pages 823-27) within metes and bounds of "a non-p300 responsive promoter"?

The art does not recognize what is meant by "a p300 responsive promoter" or "a non-p300 responsive promoter".

The specification says: Inhibition of p300 (a transcriptional coactivator) induces p53 accumulation resulting in apoptotic cell death at page 3 lines 19-21; The instant invention is drawn to the identification of p300 transactivating inhibitors which act to induce p53 accumulation through the failure to co-activate ***mdm2 at page 3 lines 25-28***; Such agent should be effective to induce apoptotic cell death for the treatment of proliferative disorders associated aberrant cell death at page 3 lines 29-31; A recombinant cell line comprising the three different plasmids plus another plasmid encoding wild-type p300 recited in the instant claims is reiterated at page 4 lines 1-12, and again at page 4 lines 19-24; Cell Lines at page 22 are generated by transfecting "the mdm2 promoter, operably linked to a reporter gene such as CAT" (lines 26-27); the cell lines with the mdm promoter linked to a reporter gene is further transfected with a control and then used for screening compounds at page 23; mdm2 promoter is an example of p300 regulated promoter at page 22 lines 24 and 25. The disclosures in the specification suggest that mdm2 promoter *might be* "a p300 responsive promoter" although it is not clear. Figures 1-30 do not show any data using a recombinant cell comprising "a p300 responsive promoter" and "a non-p300 responsive promoter".

Lill et al (June 19, 1997, Nature Vol. 387, pages 823-27), Arany et al (a copy provided with the search report, November 1997, Proc. Natl. Acad. Sci. USA, vol. 93, pages 12969-12973), and Gu et al (June 19, 1997, Nature Vol. 387, pages 819-823) all teach that p300 is a transcriptional adapter that associates with many different proteins

involved in regulating transcription of many different genes. Since p300 is involved in transcriptions of many different genes and it does not seem to directly interact with any specific DNA element and its' mechanism of action (note the introduction of Arany et al (a copy provided with the search report, November 1997, Proc. Natl. Acad. Sci. USA, vol. 93, pages 12969-12973) still known, it is not trivial to tell which promoter is more active in presence of p300 and which promoter is not responsive to p300.

The specification at Figures 1-30 does not show any data using a recombinant cell comprising "a p300 responsive promoter" and "a non-p300 responsive promoter" and does not give any example using a recombinant cells transfected with the three plasmids recited in instant claims 1-3, it is quite confusing what is meant by the claims.

For the purpose of this office action, this examiner will assume that "a non-p300 responsive promoter" is a DNA sequence whose promoter activity measured by a reporter gene is not increased by p300/CBP co-activators while "a p300 responsive promoter" is a DNA sequence whose promoter activity measured by a reporter gene is increased in presence of p300.

However, this treatment does not relieve applicant the burden of responding to this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lill et al (June 19, 1997, Nature Vol. 387, pages 823-27), Gu et al (June 19, 1997, Nature Vol. 387, pages 819-823), or Arany et al (a copy provided with the search report, November 1997, Proc. Natl. Acad. Sci. USA, vol. 93, pages 12969-12973), and further in view of

US Pat 5,607,967 and Gurtu et al (1996, Biochemical and Biophysical Research Communications Vol. 229, pages 295-298).

Claim 1 is interpreted as drawn to a stably transfected recombinant cell comprising a plasmid expressing a DNA enhancer/promoter whose activity is increased in presence of p300, linked to a reporter gene and a control plasmid expressing a DNA enhancer/promoter whose activity is not increased in presence of p300, linked to a reporter and claim 2 is interpreted as drawn to the cell lines of claim 1 further expressing a stably transfected wild-type p300, and claim 3 is drawn to method of screening useful compounds capable of regulating apoptosis using the cell line of claim 1.

Gu et al (June 19, 1997, Nature Vol. 387, pages 819-823) teach a recombinant cell transiently transfected with a plasmid expressing the mdm2 promoter operatively linked to a reporter gene, luciferase reporter gene and a second plasmid expressing p300/CBP at Figure 3 and page 820 left column second paragraph from bottom. Gu et al further teach that CBP/p300 together with the tumor suppressor p53 increases the mdm2 promoter activity. Note Figure 2.

Lill et al (June 19, 1997, Nature Vol. 387, pages 823-27) teach, at page 823 right column and Figure 2, recombinant cells comprising two plasmids, either a plasmid expressing a promoter (a consensus p53 binding site) operatively linked to a reporter gene, CAT reporter gene, i.e. PG13-CAT, and a second plasmid expressing wild-type p300/CBP or a plasmid expressing a mutated promoter operatively linked to a reporter gene, CAT reporter gene, i.e. MG_{15}-CAT, and a second plasmid expressing wild-type p300/CBP promoter.

Arany et al (a copy provided with the search report, November 1997, Proc. Natl. Acad. Sci. USA, vol. 93, pages 12969-12973) teach that recombinant cells expressing plasmids, i.e. the first plasmid expressing a DNA enhancer/promoter whose activity is increased in presence of p300, linked to a reporter gene and a plasmid expressing wild-type p300) a second control plasmid expressing a DNA enhancer/promoter whose activity is not increased in presence of p300, linked to a reporter and a third plasmid expressing wild-type p300. Note Fig. 3, abstract, page 12971, left column, and page

12970 left column under subtitle Transient transfection. Arany et al further teach p300 protein complex that activates transcription could be a therapeutic target for treatment of caner. Note the last paragraph of the article.

None of the above three references teaches screening assay for finding useful compounds using a chimeric reporter linked to a inducible promoter.

However, US Pat 5,607,967 teaches screening method using a recombinant cell comprising a promoter linked to reporter gene from column 11 line 35 to column 15 lines 50.

None of the above four references teaches a stably transfected recombinant cells expressing two reporter genes and a selectable marker gene.

However, Gurtu et al teach that stable transfection of mammalian cells is a widely used technique before the effective filing of the instant application, and an antibiotic selective marker is necessary for selection of clones with desirable stable transfection and/or maintaining selective pressure during clonal expansion. Note the abstract, the last two paragraphs. Gurtu et al further teach at Figure 4 that the reporter makes it easier to select the desirable clones; this teaching suggests that if two different reporter genes are used, then it is less time consuming and more straight forward to select clones that are transfected with multiple plasmids.

The prior art therefore teaches:

1) a plasmid expressing a DNA enhancer/promoter whose activity is increased in presence of p300, linked to a reporter gene.
2) a control plasmid expressing a DNA enhancer/promoter whose activity is not increased in presence of p300, linked to a reporter gene.
3) a selective marker plasmid.
4) a plasmid expressing wild-type p300.
5) two different reporter gene.
6) screening assays for identifying useful compounds using a reporter gene linked to enhancer/promoter element.
7) to generate stably recombinant cells.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a stably transfected recombinant cell lines using the plasmids taught by Gu et al, Lill et al, and/or Arany et al because stably transfected recombinant cells eliminate the need to transiently transfect the necessary plasmids constantly, thus saves time and eliminates tedious laboratory procedure of constantly transfecting plasmids. Further, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine teachings of US Pat 5,607,967 which teaches use of a chimeric DNA construct for screening a compound, and other references above to use the stably transfected cell lines to screen compounds that might be useful for treating cancer in the light of the teaching of Arany et al that p300 protein complex could be a therapeutic target for treatment of cancer and in light of teachings of Lill et and Gu et al that p300 is involved in p53 (tumor suppressor) regulated transcription.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
September 8, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1600